

REMARKS

Claims 1 and 3 to 45 are pending. Claims 1 and 3 to 20 are currently under consideration and claim 2 was previously canceled. Claims 21 to 45 are withdrawn. Claim 1 is currently amended.

Claim Amendments

Claim 1 has been amended to clarify that the polymer is a random polymer. Support for this amendment is found at least at paragraph [0031] and in the Examples of the application as originally filed. This claim has also been amended to specify that the polymer exhibits a discontinuous swelling ratio around a lower critical solution temperature. Support for this amendment is found at least at paragraph [0061] and [0097] and in Figure 3 of the application as originally filed.

It is believed no new matter has been added by these amendments.

35 USC 103 Rejections

(i) *Gan et al. and Vakkalanka et al.*

The Examiner rejected claims 1 and 3 to 13 under 35 USC 103 as being unpatentable over the combination of cited references Gan et al. in view of Vakkalanka et al.

Applicants respectfully submit that these claims are patentable over the cited references, for at least the following reasons.

Independent claim 1 as currently amended is directed to a process for preparing a random thermosensitive nanoporous polymer comprising polymerizing a microemulsion comprising a first monomer that is capable of forming a thermosensitive polymer and a polymerizable surfactant, wherein the polymer exhibits a discontinuous swelling ratio around a lower critical solution temperature.

The Examiner is of the opinion that in view of Vakkalanka et al., a skilled person would merely consider that the formation of a random block copolymer containing the

monomer capable of forming a thermosensitive polymer would require a higher concentration of the monomer capable of forming a thermosensitive polymer, but would eliminate a step of forming blocks of monomers for incorporation into a block copolymer.

Vakkalanka et al. relates to polymerization of hydrogels using conventional aqueous polymerization methods in the absence of polymerizable surfactant, while Gan et al. refers to polymerization from a microemulsion using a polymerizable surfactant, but does not use any monomer capable of forming a thermosensitive polymer. The Examiner appears to be of the opinion that a skilled person would expect that combination of the Gan et al. reference with the Vakkalanka et al. reference would require an increase in the concentration of monomer capable of forming a thermosensitive polymer in order to see the effect of Vakkalanka et al. in the system of Gan et al.

Applicants submit that the Vakkalanka et al. reference does not indicate whether the copolymers exhibit a discontinuous swelling ratio around a lower critical solution temperature and does not suggest that the polymers would have such a feature, which is recited in claim 1 as currently amended. Thus, the combination of the Vakkalanka et al. reference and the Gan et al. reference does not describe, disclose or suggest all of the features of the claims as currently amended.

Furthermore, there is no reason that a skilled person would expect that adding a monomer capable of forming a thermosensitive monomer to a microemulsion together with a polymerizable surfactant would successfully result in a thermosensitive, nanoporous polymer exhibiting a discontinuous swelling ratio around a lower critical solution temperature, as specified in amended claim 1.

In addition, Applicants provide the enclosed Allen et al. reference (PNAS 2003 100 (11):6331-6336) for the Examiner's consideration. The Allen et al. reference describes polymers for use as a cell growth substrate having various ratios of NIPAAm and NtBAAm. The Allen et al. reference discloses that increasing the concentration of NIPPA relative to

NtBAAM has a negative effect on the ability of the polymers to support cell growth (see for example page 6334 of the Allen et al. reference). Given that the present application describes thermosensitive nanoporous polymers that are useful as a wound dressing and as a vehicle for culturing cells for delivery of to a graft site, Applicants submit that the disclosure of Allen et al. relating to the effect of altering concentrations of NIPPAM on the polymers as a substrate for cell adhesion and growth is relevant to the present application and to the Examiner's contention that the concentration of monomer capable of forming a thermosensitive polymer could simply be increased.

Allen et al. also indicates that it is "not trivially obvious" that the surface properties of the polymer necessarily reflect the bulk properties of the polymer (see the paragraph that bridges pages 6332 and 6333 of Allen et al.), and that even altering a single surface characteristic without significantly altering the bulk properties of the polymer can affect cellular response to the polymer (see top of page 6336 of Allen et al.). Further, Allen et al. describes that "discrete modifications with respect to the physiochemistry of soft amorphous materials can lead to significant impacts on the phenotype of interacting cells" (see final paragraph of Allen et al.). Applicants submit that the Vakkalanka et al. supports this disclosure of Allen et al., since without increasing the total amount of NIPAAm, but merely reorganizing the structure of the polymer, the polymer thermosensitive properties are altered, as indicated on page 224 of Vakkalanka et al.

Based on the disclosure of Allen et al., Applicants submit that it would not be obvious that combining Vakkalanka et al. (a thermosensitive polymer that is not nanoporous and that, according to the Examiner, discloses that elevated concentrations of monomer capable of forming a thermosensitive polymer would be required when randomly polymerizing the components in order to maintain thermosensitivity in the final polymer) with Gan et al. (disclosure of a nanoporous polymer, and which reference does not describe, disclose or suggest thermosensitive polymers) would necessarily yield a polymer that retained nanoporosity and thermosensitivity and that would exhibit a discontinuous swelling ratio around a lower critical solution temperature. That is, in changing the surface properties of a

thermosensitive polymer to a nanoporous polymer, a skilled person would not have a reasonable expectation of success that thermosensitivity would be retained, particularly since Vakkalanka et al. itself indicates that changing the surface property from a block copolymer to a random copolymer has a significant effect on the thermosensitive property of the polymer. Nor would the skilled person have a reasonable expectation that the polymer would exhibit a discontinuous swelling ratio around a lower critical solution temperature, since this feature is not recited in any of the cited references.

Accordingly, Applicants submit that the combination of Gan et al. and Vakkalanka et al. do not render obvious claim 1 as currently amended and claims 3 to 13 which depend from claim 1.

(ii) *Gan et al., Vakkalanka et al. and Liu et al.*

The Examiner rejected claims 14 to 20 under 35 USC 103 as being unpatentable over the combination of cited references Gan et al. and Vakkalanka et al. and further in view of Liu et al.

Applicants respectfully submit that these claims are patentable over the cited references, for at least the following reasons.

Claims 14 to 20 each depend indirectly from claim 1 and incorporate all of the features of independent claim 1. As stated previously, and in light of the above arguments, Liu et al. does not compensate for the defect in the combination of the Gan et al. reference and Vakkalanka et al. reference.

The Examiner cited *In re Peterson* (65 USPQ 2d 1379) for the proposition that a slight overlap in range establishes a *prima facie* case of obviousness. However, in *In re Peterson*, the court held that each of the three cited references Shah, Wukusick and Bieber disclosed ranges of elements that overlapped the claimed elements.

First, Applicants point out that the *In re Peterson* case is in contrast to the present case, since none of Gan et al, Vakkalanka et al, or Liu et al. each of the claimed elements (let alone ranges for each element), as acknowledged by the Examiner.

Second, Applicants point out that even where a given reference discloses some of the elements of each of claims 14 to 20, the ranges for certain elements between the three references are not consistent with each other. For example, while Gan et al. describes HEMA in amounts between 10 and 21.25 % and Liu et al. describes HEMA in amounts between 15.68 and 23.56 % (based on 47.5% of the total mixed monomer), Vakkalanka et al. describes HEMA at 74%, which is quite different than the other two references. This difference is notable, since Vakkalanka is the only one of the three cited references that describes the use of NIPAAm, and further also includes acrylic acid, which is absent from the other two cited references. (Applicants note that the present application, Gan et al. and Liu et al. report concentrations in wt%, while Vakkalanka et al. describes concentrations in molar ratios. Vakkalanka specifically reports the use of a solution of NIPAAm:water with a molar ratio of 1:10, and a molar ratio of NIPAAm:acrylic acid:HEMA of 10:10:80 (see first paragraph under heading "Experimental" on page 222, the first and second full paragraphs on page 224, and the figure legend of Figure 2 on page 223), resulting in a molar ratio of 1:1:8:10 of NIPAAm:acrylic acid:HEMA:water, or % w/w of approximately 8%, 5%, 74% and 13% for NIPAAm, acrylic acid, HEMA and water, respectively (based on respective molecular weights of 113 g/mol, 72 g/mol, 130 g/mol and 18 g/mol).)

Thus, Applicants submit that a skilled person, having regard to Gan et al., Vakkalanka et al., and Liu et al., would not arrive at the specific components and concentrations of claims 14 to 20, particularly given the discrepancies between the three cited references, given the fact that none of the cited references discloses ranges for each element within claims 14 to 20, given that the one reference that does include NIPAAm (Vakkalanka et al.) also includes acrylic acid and given the disclosure of Allen et al. which indicates that even keeping bulk properties essentially unchanged, changes in surface properties can have a significant effect on the polymer properties and effect. Thus, Applicants submit is not a matter of simply

selecting the amount of each component from a range within a single reference as was the case in *In re Peterson*.

Thus, in addition to the comments provided above for the combination of Gan et al. and Vakkalanka et al., Applicants submit that further combination of the Liu et al. reference does not render the presently claimed processes of claims 14 to 20 as obvious.

(iii) *Gan et al. and Lee et al.*

The Examiner rejected claims 1 and 3 to 13 under 35 USC 103 as being unpatentable over the combination of cited references Gan et al. in view of Lee et al.

The Lee et al. reference describes polymers comprising NIPAAm, acrylamide and HEMA. The Examiner is of the opinion that it would have been obvious to a skilled person to use the NIPAAm from the Lee et al. reference and combine it with the Gan et al. reference.

Applicants respectfully submit that these claims are patentable over the cited references, for at least the following reasons.

The Lee et al. reference includes both NIPAAm monomers and acrylamide monomers (along with HEMA monomers) to create polymers that are both temperature sensitive and pH sensitive and thus have differing swelling responses as both temperature and pH vary.

Lee et al. does not describe, disclose or suggest that the polymer exhibits a discontinuous swelling ratio around a lower critical solution temperature. In fact, Applicants submit that the results described in Lee et al. suggest that the polymers exhibit a continuous swelling ratio along a temperature gradient (see for example Figures 1, 3 and 4 of Lee et al.).

Applicants submit that the NIPAAm monomers are included in Lee et al. in order to add a temperature sensitivity aspect to the pH sensitivity of the acrylamide component of the polymer. This can be seen in the results displayed in Figure 1. In that Figure, each of panels

(a), (b), (c) and (d) relate to a different polymer, with panel (a) displaying the results of the polymer having the highest NIPAAm content (X1) and panel (d) displaying the results of the polymer having the lowest NIPAAm content (X7). As can be seen in Figure 1, as NIPAAm concentration is decreased, the swelling ratio of the polymers becomes more temperature sensitive at pH 10.4 (upper two curves in each graph move farther apart). The swelling at pH 10.4 appears to be related to the ionic state of the acrylamide and not directly due to the NIPAAm, since swelling increases as temperature increases (the top curve is 45°C, indicating that the polymers swell more going from 25°C to 45°C), which is the opposite of expected if the swelling was in response to the LCST of NIPAAm. This is indicated at the top of page 225, second column, where the reference states, "According to these results, ΔSR is controlled mainly by the AAm content in the gels."

The Examiner points to the statement on page 225 of the Lee et al. reference that the temperature-sensitive character of the NIPAAm-AAm-HEMA gel series is influenced mainly by the amount of NIPAAm in the networks. Applicants note that this statement is made in reference to the results at pH 4, rather than to all of the results. Furthermore, Applicants point out that in light of the Allen et al. reference described above, it would not be apparent to a skilled person that combining a polymerizable surfactant in a microemulsion together with a monomer capable of forming a thermosensitive polymer would result in a thermosensitive, nanoporous polymer that exhibits a discontinuous swelling ratio around a lower critical solution temperature, as provided in claim 1 as currently amended. The Lee et al. reference studies the effect of thermosensitivity in the context of pH sensitivity, and does not describe a discontinuous swelling ratio around a lower critical solution temperature.

Thus, in light of the description of Lee et al. relating to a combination of thermosensitivity and pH sensitivity, the absence of any description relating to a discontinuous swelling ratio around a lower critical solution temperature, and in light of the Allen et al. reference, Applicants submit that the presently amended claims are patentable over the combination of the Gan et al. reference and the Lee et al. reference.

(iv) *Gan et al., Lee et al., and Liu et al.*

The Examiner rejected claims 14 to 20 under 35 USC 103 as being unpatentable over the combination of cited references Gan et al. and Lee et al. and further in view of Liu et al.

Applicants respectfully submit that these claims are patentable over the cited references, for at least the following reasons.

Claims 14 to 20 each depend indirectly from claim 1 and incorporate all of the features of independent claim 1. As stated previously, and in light of the above arguments, Liu et al. does not compensate for the defect in the combination of the Gan et al. reference and Lee et al. reference.

As stated above, Applicants submit that the *In re Peterson* case does not apply to the present application, for the reasons stated above.

As with the previous combination, the ranges given in the Lee et al. reference are not consistent with the Gan et al. reference and the Liu et al. reference. For example, while Gan et al. describes HEMA in amounts between 10 and 21.25 % and Liu et al. describes HEMA in amounts between 15.68 and 23.56 %, Lee et al. describes HEMA at 2.3 % (based on the given weight as a percentage of the combined weight of all the elements, including 8 g of water/ethanol solution, as described). This is in combination with acrylamide, which is a monomer that imparts pH sensitivity, which type of monomer is not present in the listed components of claims 14 to 20. As with the Vakkalanka et al. reference, the Lee et al. reference is the only reference the only one of the three cited references in this reference combination that describes the use of NIPAAm, and further also includes acrylamide, which is absent from the other two cited references.

Additionally, the Lee et al. reference stands in contrast to the Vakkalanka et al. reference, teaching different combination of components and amounts for each component. The amounts of NIPAAm in Lee et al. range from approximately 5.2% to 0.7% with

acrylamide ranging from approximately 1.6 to 2.9 % w/w, HEMA at approximately 2.3 % w/w, and water and ethanol each at approximately 23 % w/w, whereas the Vakkalanka et al. references describes NIPAAm:acrylic acid:HEMA:water at % w/w of approximately 8:5:74:13.

The description of the Allen et al. reference further underscores the discrepancies between the cited references and the present claims 14 to 20.

Thus, Applicants submit that a skilled person, having regard to Gan et al., Lee et al., and Liu et al., would not arrive at the specific components and concentrations of claims 14 to 20, particularly given the discrepancies between the three cited references, given the discrepancies between the Lee et al. reference and the Vakkalanka et al. reference, given the fact that none of the cited references discloses ranges for each element within claims 14 to 20, given that the one reference that does include NIPAAm (Lee et al.) also includes acrylamide (which imparts pH sensitivity) and ethanol, and given the disclosure of Allen et al. which indicates that even keeping bulk properties essentially unchanged, changes in surface properties can have a significant effect on the polymer properties and effect. Thus, Applicants submit is not a matter of simply selecting the amount of each component from a range within a single reference as was the case in *In re Peterson*.

Thus, in addition to the comments provided above for the combination of Gan et al. and Lee et al., Applicants submit that further combination of the Liu et al. reference does not render the presently claimed processes of claims 14 to 20 as obvious.

In summary, based on all of the above arguments, Applicants submit that claim 1 as amended and claims 3 to 20 which depend directly or indirectly from claim 1 are patentable over each of the combination of cited references and respectfully request withdrawal of the rejections under 35 USC 103.

Information Disclosure Statement

The Examiner commented that the information disclosure statement filed June 10, 2009 is non-compliant due to either a missing statement under 37 CFR 1.97(e) or a missing fee. Applicants point out that the information disclosure statement included a deposit account charge authorization to satisfy the fee requirement. Accordingly, Applicants respectfully request that the Examiner consider the contents of the information disclosure statement filed June 10, 2009. For convenience, a copy of the previously submitted form PTO/SB/08b, listing the Antonietti publication, is being submitted herewith.

Conclusion

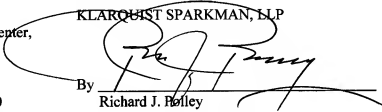
Applicants respectfully request entry of this amendment, favourable consideration and withdrawal of the rejections.

Respectfully submitted,

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